REMARKS

Applicants' response to the pending Restriction Requirement and discussion of claim amendments appear below.

Claims 1-5, 7-10, 13, 14, 20, 21, 31, 51 were subjected to a restriction/election requirement. Of these, claims 4 and 8 have been elected, and linking claims 1-3, 7 and (previously presented claim) 41 remain active in this case.

Claims 6 and 17 (whose group was not elected) are canceled without prejudice or disclaimer of the subject matter therein.

Some of the amendments have been made to clarify the language of the claims or to correct typographical /clerical errors. Specific amendments are discussed in Section II, below.

Support for the amendments can be found in the original claims as well as throughout the specification. No new matter has been added by these amendments.

I. RESTRICTION/ELECTION REQUIREMENT

Applicants thank the Examiner Wang and SPE Andres for the courtesy of a telephonic interview to discuss the Restriction Requirement and the interpretation of claim 1 as lacking unity, based on the Office's view that claim 1 read on two prior art references. While Applicants do not agree with the interpretation of the scope of earlier claim 1, they have carefully amended this claim to reflect their original intention that it encompass only particular fragments of the known PLP/DM20 protein disclosed in the two cited references, and not read on the full length proteins. It is believed that claim 1 is patentable over the prior art, and thus can be treated as a proper linking claim for the claims of Group I being elected herein.

A. ELECTION OF INVENTION:

Applicants elect Group I, claims 4 and 8, drawn to the PIRP-M polypeptide (SEQ ID NO:6) or the His-tagged PIRP-M polypeptide (SEQ ID NO:12), with traverse. Applicants' discussion of the Restriction Requirement and their request that it be modified with respect to certain (non-elected) groups is found in Section I, B. Applicants understand that Claims 1, 2, 3, 7 and 41 are considered to be linking generic claims in relation to the embodiments claimed in the Group 1 claims. Applicants believe that claim 2(c), and claims 3, 7 and 41 (in part) should be considered together

with Group I, to the extent that they read on the PIRP-M polypeptide (SEQ ID NO:6) alone or as a fusion partner.

In any case, Applicants understand that the Restriction Requirement among linked inventions is subject to the nonallowance of these linking claims. Upon the indication of allowability of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowable linking claims will be rejoined and fully examined for patentability.

Applicants understand this to mean that if claims 4 and 8 are found to be allowable, the Office will extend the examination to the linking claims to include the additional embodiments therein (other PIRP-M fusion proteins, PIRP L polypeptides and fusion proteins, and the PIRP-J polypeptide, pharmaceutical compositions comprising such polypeptides) up to the full scope of amended claim 1.

B. Request for Modification of Definition of Groups

For convenience, Applicants will refer to the claimed PLP-derived polypeptide fragments by the designated names PIRP-M and PIRP-L (and PIRP-J) as well as indicating the relevant SEQ ID NO's. Applicants respectfully remind the Office that "optimized" nucleic acid sequences encode the identical polypeptide as do their respective native nucleic acid sequences. Note also that PIRP-L is an internal fragment of PIRP-M and both have been found to possess the same biological activities.

The Applicants believe that certain of the claim groupings are based on inadvertent clerical error as discussed briefly during the telephonic interview of October 17, 2006. Applicants believe that the Examiner's meant to group some of the claims differently, particularly Groups IV-VIII, as set forth in the Table and discussion below. Applicants also draw the examiner's attention to the indication of the appropriate linking claims common to the polynucleotide embodiments of Groups IV-VIII.

Another regrouping is requested based on an inadvertent error by Applicants in the present claim set (where claims 50 and 51 were identical). This has been corrected by amendment. Furthermore, Applicants have commented below on Groups X, XIII and XVI. These requested modifications are important for either later rejoinder or for defining the proper groups for future divisional applications.

To summarize, Applicants hereby request that the groupings be reconsidered and modified as follows:

Group IV: Claim 15 in full (SEQ ID NO:5 or 9) and claim 18 (SEQ ID NO:11)

Group V: Claim 16 in full (SEQ ID NO:7 or 13) and claim 19 (SEQ ID NO:15)

Group VI: no longer necessary as its "contents" have been moved to Group V

Group VII: no longer necessary as its "contents" have been moved to Group V

Group XI: Claim 50 in full; claim 56 in full

Group XII: Claim 51 in full;

Group XIII: claims 52-54 - all use the polypeptide of claim 4 (PIRP-M) to "help" cells that are on the differentiation pathway from neural stem cells to oligodendrocyte precursors to mature oligodendrocytes. The claimed methods do the following:

Claim 52 stimulate neural stem cell survival and promote their differentiation/ maturation along the oligodendrocyte pathway;

Claim 53 stimulate proliferation of oligodendrocyte precursors or oligodendrocytes; and

Claim 54 protect oligodendrocytes from apoptotic death.

Applicants do not understand why Group XIII is limited to these claims "in part" and request that the Restriction be modified to indicate that the invention includes these claims "in full." Applicants also do not understand why "*in vitro*" limitations were read into these claims by the Office (per the Office's description of Group XIII) since these claims read on methods conducted *"in vivo"* as well as *"in vitro."*

Applicants believe it would be proper to combine Groups XV and XVI as claims 59 and 60 recite methods using cells that express the indicated polynucleotides and polypeptides. Since expressing the inserted polynucleotide results in the cells' expressing the polypeptide, these should not be considered distinct inventions.

Apparent Clerical Errors in Grouping Various Polypeptides

The Table below lists various Groups, and the embodiments and sequences associated with each claim of group of claims

Claims focus	*Specific Polypeptide or Polynucleotide / Logical Groupings*	Sequences	Actual Group/ Claims	Linking claims (or comments)
Polypeptide	PIRP-M His tagged PIRP-M	SEQ ID NO:6 SEQ ID NO:12	I/ 4 and 8	1-3, 7, 41
	PIRP-L His tagged PIRP-L	SEQ ID NO:8 SEQ ID NO:16	II/ 5 and 9	
	PIRP-J	SEQ ID NO:18	III/ 6	

Claims focus	*Specific Polypeptide or Polynucleotide / Logical Groupings*	Sequences	Actual Group/ Claims	Linking claims (or comments)
Polynucleotide & Vectors	PIRP-M (native)	**SEQ ID NO:5**	IV / 15 (**not** 'in part')	10-14 20-27 ***28 dep from 27 (should be incl)*** 29-30 ***31 dep from 28 (should be incl)*** 42-43
	PIRP-M (optimized)	**SEQ ID NO:9**	V / 15 **(error) ⇒[1] IV**	
	His-tagged PIRP-M (optim)	**SEQ ID NO:11**	IV / 18 (correct)	
	PIRP-L (native)	**SEQ ID NO:7**	VI / 15 **(error) ⇒ V**	
	PIRP-L (optimized)	**SEQ ID NO:13**	VII / 15 **(error) ⇒ V**	
	His-tagged PIRP-L (optim)	**SEQ ID NO:15**	V (OK)	
	PIRP-J (native)	**SEQ ID NO:17**	VIII / 17 (OK)	
Cells	Modified to contain vectors		IX / 32-40 and 44	Dependency from claim 10 which is a linking claim for all polynucl/vector claims
Meth to treat disease (w / polypeptide)	PIRP-M	SEQ ID NO:6	X / 46-49, 52-54 (all in part), 55	Why '*in part*'?: claim 46-49 and 52-54, 55 all dep from claim 4 **(PIRP-M only)**
Meth to treat disease w / cells	Cells expr **PIRP-M** native or optimized **nucleotide** seq or **PIRP-M** polypeptide	SEQ ID NO:5 or:9 (nt) SEQ ID NO:6	XI/ 50, ~~51~~,[2] 56 (all in part)	*After correcting error by amending of Claim 51, Group XI would corresp to PIRP-M and Group XII to PIRP-L*
Meth to treat disease w / cells	***Intended Claim 51***[2] Cells expr **PIRP-L** native or optimized **nucleotide** seq, or PIRP-L polypeptide	***Amended to:*** SEQ ID NO:7 or:13 (nt) SEQ ID NO:8	XII/ ~~50~~,~~51~~, ~~56 (all in part)~~	
Meth to stimulate neural stem cells, *etc. in vitro* (?) w / polypeptide	PIRP-M	SEQ ID NO:6	XIII / claims 52-54 (all in part)	Examiner "read in" *in vitro* limitation. If *in vivo too*, couldn't these be grouped with Group X
Meth of regul or inhib prod (of PLP or of PIRP-M) *w / polypeptide*	PIRP-L	SEQ ID NO:8	XIV / 57-58	*Claims dep from claim 5 (=Group II) - which dep from linking claims as set forth for Group II*
Meth of regul or inhib (prod of PLP or PIRP-M) *w / cells*	Cells expressing native PIRP-L protein.	SEQ ID NO:7.	XV / 59-60 (all in part) *Why in part?*	*Claims dep from claim 32 which dep from claim 10 - one of the linking claims*
Meth of regul or inhib (prod of PLP or PIRP-M) w / cells	Cells expressing optimized PIRP-L nucleic acid	SEQ ID NO:13..	XVI / 59-60 (all in part) *Why in part?*	Why not grouped with XV? (cells expr nt also express PIRP-L protein)

[1] ⇒ ""should be"

[2] Claim 51 was erroneously identical to claim 50. Applicants intended the PIRP-L equivalents of claim 50 (i.e., nucleotide sequence SEQ ID NO:7 or 13 encoding aa sequence SEQ ID NO:8. Claim has been so amended (and withdrawn).

The Office's grouping of claims and sequences in Groups IV-VIII, together with Applicants' comments are presented below:

Group IV: drawn to the **polynucleotides and vectors of:**

Claims 15 (in part) PIRP-M/ SEQ ID NO:5 (native) or SEQ ID NO:9. (optimized) -
Claim 18 His-tagged PIRP-M (SEQ ID NO:11)
Claim 28 (in part) vector (generic to PIRP-M, L and J)
Claim 30 (in part), vector (generic to PIRP-M, L and J)
Claim 31 (in part) vector (generic to PIRP-M, L and J)
Included: SEQ ID NO:5 (native PIRP-M)
SEQ ID NO: 11 (His-tagged/optim PIRP-M)
Missing: SEQ ID NO: 9 (optimized PIRP-M

Group V: drawn to the **polynucleotides and vectors** of:

Claim 15 (in part) SEQ ID NO:5 (native PIRP-M) ***(already in Group IV)*** or
SEQ ID NO:9 . (optimized PIRP-M) ***(belongs in Group IV)***
Claim 19 SEQ ID NO:15 (His-tagged/optim PIRP-L)
Claim 28 (in part) vector (generic to PIRP-M, L and J)
Claim 30 (in part) vector (generic to PIRP-M, L and J)
Claim 31 (in part) vector (generic to PIRP-M, L and J)

Included: SEQ ID NO:9 (optimized PIRP-M) *(belongs in Group IV)*
SEQ ID NO:15 (His-tagged PIRP-L) *(correct)*
Missing SEQ ID NO:7 - native PIRP-L (mistakenly in Group VI)
Missing: SEQ ID NO:13 -optimized PIRP-(mistakenly in Group VII)

Group VI: **polynucleotides and vectors** of SEQ ID NO:7:

Claim 16 (in part) PIRP-L/ SEQ ID NO 7 (native) *(belongs in Group V)*
Claim 28 (in part) vector (generic to PIRP-M, L and J)
Claim 30 (in part) vector (generic to PIRP-M, L and J)
Claim 31 (in part) vector (generic to PIRP-M, L and J)

Included: SEQ ID NO:7 - native PIRP-L *(belongs in Group V with optimized and His-tagged PIRP-L)*

Group VII: **polynucleotides and vectors** of SEQ ID NO:13:

Claims 16 (in part) PIRP-L/SEQ ID NO:13 (optimized) *(belongs in Group V)*
Claim 28 (in part) vector (generic to PIRP-M, L and J)
Claim 30 (in part) vector (generic to PIRP-M, L and J)
Claim 31 (in part) vector (generic to PIRP-M, L and J)

Included: SEQ ID NO: 13 (optimized PIRP-L) *(belongs in Group V with native PIRP-L and His-tagged PIRP-L)*

Group VIII: **polynucleotides and vectors** of SEQ ID NO:17 (PIRP-J.)

Claim 17 PIRP-J/SEQ ID NO:17 *(this claim is being canceled, though the embodiment remains in the linking claims)*
Claim 28 (in part) vector (generic to PIRP-M, L and J)
Claim 30 (in part) vector (generic to PIRP-M, L and J)
Claim 31 (in part) vector (generic to PIRP-M, L and J)

C. Species Election

Because the species election required by the Office was directed to a Group not being elected here, Applicants are not respond here to this requirement.

II. CLAIM AMENDMENTS

A. Claim 1

Claim 1 has been amended so that it no longer can be considered to read on the references cited as a basis for disunity. Applicants understand that the disunity determination will not be withdrawn at this time as a result of the amendment. However, Applicants note that the Action indicates (in Sec. 3) that claims 1-3 and 7 (drawn to polypeptides or fusion polypeptides and claim (drawn to a pharmaceutical composition comprising the polypeptide of claim 1) link all the present polypeptide inventions (Groups I, II and III). The Office further stated that the restriction requirement among the linked inventions is subject to the nonallowance of these linking claims so that "

> upon the indication of allowability of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise requiring all the limitations of the allowable linking claims will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104.

Thus, in view of Applicants' election of Group I, with the present amendment of linking claims, Applicants understand that if such claims are found allowable over the art, then the Office will examine the linking claims for patentability.

Discussion of Amended Claim 1 in Connection with References Cited for Disunity

Amended claim 1 recites a fragment of PLP, that does not read on the full length PLP molecule disclosed in Folch, J. *et al.*, 1951, *J Biol Chem 191*: 807-817 and Wolfgram, F., 1966. *J. Neurochem. 13*: 461-470. Please note that the language "first amino acid sequence" and "comprising" of prior claim 1 are no longer present. Thus claim 1 is limited to (a) a fragment of a full length PLP protein (wild-type or mutant) that, because it is encoded by an IRES, has as its N-terminus an *internal* residue of the full length PLP. The claim is also directed to a fusion protein of this above novel PLP fragment. Thus, claim 1 does not read on the native full length PLP proteins disclosed in these cited references.

B. OTHER AMENDMENTS

Other claims have been amended to place their language more in correspondence with amended claim 1 or otherwise to clarify the language. Some amendments fix obvious typographical/clerical errors in the earlier claim set. Claims 6 and 17 have been canceled without prejudice or disclaimer.

Please note that a number of the amendments are made in either linking claims or withdrawn claims. Applicants did not designate the linking claims corresponding to the elected invention as being "withdrawn;" Applicants understanding of how those linking claims will be treated is stated elsewhere in this paper. Amendments to withdrawn claims are intended to keep them in correspondence with elected claims (or linking claims) for either possible later rejoinder or for submitting them in better condition in a divisional application. It is Applicants' intention to maintain and amend the withdrawn claims as the examination of this case proceeds. Once final decisions have been made as to allowable subject matter, Applicants will cancel the appropriate withdrawn claims.

Applicants also note that because the Office required restriction between product and process claims. When the elected product claims are found allowable, Applicants understand that the Office will consider for rejoinder withdrawn process claims that depend from, or otherwise include require all the limitations of the allowable product claims.

III. CONCLUSIONS

In view of the above election of invention, remarks and amendments, it is believed that the present claims are in condition for examination and allowance. Accordingly, the Examiner is respectfully requested to enter Applicants' election and amendments, modify some of the groupings of claims into separate inventions in accordance with Applicants' requests, examine the elected claims, and, upon indication of their allowability, examine and allow the linking claims for the elected invention.

If these papers are not considered timely filed by the Patent and Trademark Office, then a petition is hereby made under 37 C.F.R. § 1.136, and any additional fees required under 37 C.F.R. § 1.136 for any necessary extension of time, or any other fees required to complete the filing of this response, may be charged to Deposit Account No. 50-0911. Please credit any overpayment to deposit Account No. 50-0911.

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